FEDERAL SECURITY AGENCY
PUBLIC HEALTH SERVICE

IN REPLYING, ADDRESS THE
Tuberculosis Research Laboratory,
411 East 69th St., New York 21, N. Y.

October 10, 1951.

Dr. Joshua Lederberg,
Department of Genetics,
The University of Wisconsin,
College of Agriculture,
Madison 6, Wisconsin.

Dear Joshua:

Thanks for your letter of October 1st. To answer the questions asked therein: I would be very pleased to continue to receive any monstrosities that come your way since I seem to be developing a small factory, with the engagement of a chemist on a full-time basis soon, for isolating metabolites, and must keep a back-log of unknown factors waiting for him. The aromatic series will surely last a while longer, but not indefinitely. I am not very enthusiastic, however, about tackling unknown yeast extract factors since they are apt to be vitamins that will require tons of material to yield the amount necessary for identification. I therefore wonder whether you would mind my passing PF-11 along to Woodruff at Merck, who says they would like very much to look into unknown factors of this sort.

I presume that the W-1427 referred to in your letter of October 1st really means W-1504, the mixture of tyrosine and proline auxotrophs. While I would be inclined to interpret this as a straightforward mixture probably arising from the isolation of overlapping colonies from a penicillin experiment, I wouldn't entirely rule out the possibility hinted at in your remarks, that the original isolate might be an unstable mutation that could later settle into either being an orthodox tyrosine or an orthodox proline auxotroph. Way back we did isolate in one experiment the same mixture of two amino acid auxotrophs from two separate colonies in the same experiment, and I wondered whether this could be more than coincidence. I am afraid this meager contribution is all I could offer to support your suspicions.

We have not encountered any strain that grows in liquid medium but not on agar, and would be glad to send you some washed agar if you would care to try it.

I am afraid my reprint of your Genetics 1947 paper is so dog-eared that it wouldn't be very useful to you. You were not incorrect, however, in your assumption that I would be a purchaser of the reprint book, though I really wonder whether the publishers wouldn't spare a copy to each of the "contributors".

Dr. Joshua Lederberg October 10, 1951.

You might like to know the results of working up your tryptophan auxotrophs: W-1145 and Shapiro 1-28 grow well on indole and heavily feed the strain that responds to anthranilic. W-1069 and SW-8 are slow on indole and do not feed any other strains. There is a mystery here that I hope to look into some day. The two Pseudomonas strains, PF-20 and PF-24, respond only to tryptophan and do not feed any of our coli strains with early blocks. This failure to excrete indole, which we have also encountered in certain coli strains blocked between indole and tryptophan, is particularly interesting in view of your statement that Pseudomonas is a prolific indole producer. I presume this statement refers to action of wild type on a medium containing lots of tryptophan. Incidentally, wasn't that a beautiful paper by Roger and Hayaishi in Science last week?

Am I correct in assuming that the lysine plus methionine requirement of W-1069 arose from a single mutation? This particularly interests me since we have recently found that the POB requirement (and the POB antagonism to inhibition by its analogue) can be replaced by methionine plus lysine, or the known precursors of these two amino acids. This suggests, of course, that POB might function in the synthesis of a common precursor of these two amino acids but, unfortunately, POB has no effect as a replacement with W-1069. I am enclosing, particularly because of the evolutionary concepts invoked, a paper that I just sent off to Nature on the synthesis of lysine.

With best regards,

Sincerely yours,

Bernard D. Davis

BDD/hl

enc.